Opinion on the prescription of antiandrogenic substances to prison inmates sentenced for offences of a sexual nature.

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Opinion

Cyproterone acetate (Androcur) and tryptoreline (Decapeptyl) are two molecules, that are capable, by different mechanisms, of weakening sexual desire (libido) in men, in a reversible manner.

Androcur is a testosterone antagonist steroid (testosterone being a hormone secreted by the interstitial cells of the testicle, and on which primary and secondary sexual characteristics, and spermatogenesis all depend).

Decapeptyl is a " hyperactive" analogue of a hypothalamic hormone, that drives the anterior pituitary gland's secretion of gonadotropic hormones, one of which stimulates the testicle's secretion of testoterone. The administration of Decapeptyl, after a phase of stimulation, results in desensitisation of the anterior pituitary gland, with consequent collapse of testosterone secretion.

These two molecules have many therapeutic indications, notably for the treatment of prostate cancer, and, in women, the treatment of certain breast cancers.

There are quite a few foreign references concerning the use, in a non-prison environment, of Androcur (at doses far below those used in cancer treatment) to prevent relapses of sexual offenders. The overall results appear to be favourable, especially when the subject is provided with psychiatric support. The use of Decapeptyl is much less well documented; it is used mostly in Canada.

However, the effectiveness and the long-term tolerance of these substances are not sufficiently well known, which is good grounds for submitting their administration to therapeutic trials. Such trials require free, informed and expressed consent, all of which conditions may not be fulfilled in a prison environment, so that the initial phase of administration should be considered a medical prescription, with the trial as such beginning as of the inmate's release.

To the extent that the administration is a medical prescription, the National Consultative EthicsCommittee is not competent to pronounce itself. Nevertheless, it considers that, if the administration of these products is to be continued, it necessarily includes the two phases mentioned above. Therefore the Committee considers itself entitled first to take a stand on the initial modalities of their administration.

The concept of " free and informed consent" immediately takes on very great importance, with the meaning of both qualifiers counting to the hilt.

- informed: The inmate must know that this is not a systematic and commonplace prescription, and that the time perspective is not yet sufficient for completely satisfactory results to be assured. He has to be informed of the temporary diminishing effect on his libido, but without him having to fear permanent impotence. Finally, he must be apprised of the fact, that his acceptance will be required after his release.

- free: At first blush, it may seem paradoxical to speak of freedom with respect to the decision of an inmate. But if the date of his release is not far off, he would no longer be hoping to gain any advantage as a consequence of his cooperativeness.

The requirement of free and informed consent must be supplemented by a requirement of expression of the consent, when the second phase is launched. This consent has to be authentified by an explicit formulation of acceptance, written out and signed by the former inmate.

This second phase would take the form of a therapeutic trial, carried out under the conditions established by the law of December 20th 1988. The research aim would be to improve understanding of the consequences, over a long period, of the administration of the product:

- on the one hand, as the foremost aim, for the protection of potential victims, especially minors,

- on the other hand, for the possibility of the subject's return to some form of sexual activity, and in terms of the absence of side effects with potential harm to the treated subject's health.

The application of prevailing legal instruments requires the formulation of a new consent, as part of an experimental protocol.

The following two conditions need to be added:

- While the prescription proposal may be advanced by a physician of the penitentiary administration, the therapeutic trial must definitely be conducted by a practitioner external to that administration. This provides an additional guarantee of freedom of consent. Moreover, this distinction between the two phases will keep the subject from having to return to the prison environment after his release.

- In the absence of any possibility of mandatory examination of subjects, the results of trials will have to be submitted to a multi-disciplinary effectiveness evaluation. In this respect, several factors will have to be taken into consideration: the potential danger of stopping administration of the substance, the frequency of relapses, and the physical and mental consequences for persons having agreed to participate in the trial.

Report

The General Inspectorate of Social Affairs (Inspection générale des affaires sociales - IGAS) has sollicited the opinion of the National Consultative Ethics Committee on the following point:

" In the case of inmates sentenced for crimes or offences of a sexual nature, and when the risk of serious relapse is high, may they be subjected, and under what conditions, to a

prescription by physicians, connected with the penitentiary institution, of substances such as Decapeptyl or Androcur, when the sole objective is to inhibit their libido?"

This question is doubtless motivated by the constant increase in the number of crimes and offences of a sexual nature, and in the number of inmates sentenced to ever longer terms for this type of violation of the law.

I - Modes of action and primary therapeutic indications of Decapeptyl and Androcur

Decapeptyl is the commercial name of a synthetic decapeptide, triptoreline, whose structure is close to that of a hypothalamic hormone, namely LHRH (Luteinizing Hormone Releasing Hormone), so called because it stimulates the anterior pituitary gland's release of LH (Luteinizing Hormone), which plays a major role, in women, in ovulation and corpus luteum formation.

In men, LH (also and more logically called ICSH, or Interstitial Cell Stimulating Hormone) stimulates testosterone secretion by the interstitial cells of the testicle. Testosterone is an androgenic hormone through its action on primary and secondary sexual characteristics, on spermatogenesis and on sexual behaviour.

Under physiological conditions, LHRH secretion is discontinuous. When administered intermittently in order to imitate natural secretion, LHRH stimulates sustained secretion of gonadotropins, including LH. On the other hand, continuous administration results, after a transitional phase of stimulation, in desensitization of the anterior pituitary gland, causing LH secretion to stop, and consequently, in men, testosterone secretion to collapse.

Decapeptyl is one of the group of substances called " hyperactive analogues" or " super-agonists" , because certain differences in their structure, with respect to that of biological molecules, endows them either with much stronger affinity for the receptors of these molecules, or with greater resistance to the enzymes that inactivate them. As a result, Decapeptyl administered in single doses has the same inhibiting effects as LHRH administered continuously.

Decapeptyl is used to treat prostate cancer and certain breast cancers, as well as in the case of endometriosis and precocious puberty. In men, symptoms associated with testosterone deficiency have been observed in the course of such treatments: significant weakening of the libido, impotence. It is these " side" effects that can make this substance an antidote to the violent impulsions that lead to offences of a sexual nature.

Androcur, the commercial name for cyproterone acetate, is a testosterone antagonist steroid. Its antiandrogenic effect results from competitive inhibition, exercised throughout the target cells, of the bond between testosterone and its receptors. When used to treat prostate cancer and certain skin diseases (severe seborrhea, acne), Androcur also results, at therapeutic doses, in a significant weakening of the libido with impotence and gynecomastia, as well as inhibition of spermatogenesis, possibly leading to temporary sterility.

So it is through very different mechanisms that these two substances bring about a substantial weakening of the effects of testosterone, which has the advantage of being reversible. When administered at doses substantially smaller than therapeutic doses, these substances seem to be able to subdue libido significantly, without resulting in impotence.

II - Legal and ethical considerations regarding the administration of Androcur and Decapeptyl to inmates

To begin with, three observations need to be made:

1) The prescription of Decapeptyl to inmates serving sentences for offences of a sexual nature is far from widespread across the many penitentiary institutions, where such offenders, who fall into very different categories, are incarcerated. Such prescription is still exceptional. Moreover, not much is known about the overall effect, for this particular indication, of these products, which are usually administered for different pathologies. It should be noted that Decapeptyl, because of the initial phase of excitation it may provoke, requires special monitoring, in particular when taken in association with Androcur.

2) In so far as the legal aspect is concerned, Article D380, Paragraph 4, of the Code de procédure pénale (Code of Criminal Procedure) stands in the way of trials on inmates, but on the other hand, Article L209-5 of the Code de la santé publique (Public Health Code), based on law N° 88-1138 of December 20th 1988, on the protection of persons who consent to biomedical research, authorises such trials under certain conditions. This is a difficulty which we can only highlight.

3) Assuming that one accepts the second of these texts, the administration of the substances in question for the purpose of research is possible, but it is also necessary that " a major and direct benefit" for the subject's health be reasonably expected. There is no doubt that this requirement is satisfied, for this is precisely the sort of benefit that is " expected" .

III - This having been established, there are two ways of approaching the problem: the use of these products in a trial or their use in two stages, with treatment followed by a trial

The use of these products in a trial

1) The law cited above must be observed with particular vigilance, especially in so far as consent is concerned. The modalities of such consent, which must be free, informed and expressed in any event, take on very special significance under these circumstances. One could even argue that it is illusory to speak of freedom of consent for an inmate. The concept of freedom requires that there be no association whatsoever between the stand adopted by the inmate, and his fate in detention or the length of his term in prison.

This is one of the reasons why there can be no question of proposing these products before the latter part of the sentence, in order that there be no possibility of giving consideration to a pardon or to early release under parole; this means that their prescription at the beginning of incarceration is to be excluded, and that they cannot be offered in the course of the sentence, save under exceptional circumstances.

In the second place, the interested person must have full knowledge of the path he is taking: temporary reduction of his " libido" , obligation to continue the treatment after release, whether orally or by injection, and to submit to periodic medical examinations, especially for psychiatric care.

Finally, the consent must be given in writing. These conditions could well be supplemented by a requirement for the inmate to have a meeting, before agreeing to treatment, with a person of his choice from outside the penitentiary administration (for example, a lawyer).

Given the evolutionary and uncertain nature of the results, and in order to be sure of the

subject's firmness of resolve, it is advisable to have him give his consent twice over, once before and a second time during administration of the product.

We are confronted here with tensions, that are difficult to reconcile, between respect for the individual and the protection of individuals. The first requirement means that the subject having given his consent must be granted the freedom to withdraw it at any time. The second consent actually amounts to a measure demonstrating re-affirmed awareness on the part of the subject at a certain stage of the process. The second requirement, which is of capital importance, involves a constant concern for social protection, through an effort aimed at reducing the threat to potential victims, in particular children.

2) After it is drawn up, the protocol has to be submitted to the competent committee for the protection of subjects in biomedical research.

3) While the prescription proposal can be made by a physician of the penitentiary administration, the treatment, on the other hand, can only be undertaken and continued by a physician independent of that administration. This is an additional guarantee of freedom of consent. Moreover, this distinction between the phases ensures that the inmate will not have to return to the penitentiary environment after his release.

4) We are speaking of trials. Consequently, there must be a final evaluation. It will teach some useful lessons, to the extent that the experience gained is encompassed within a formal programme, and then confronted and compared. Thus it is advisable, after a set period of time, to establish a general orientation, with a view to determining whether recourse to these substances can become common practice, and if so, under what conditions.

Use of the substance in two stages, with treatment followed by trial

Under this option, the preceding analysis ought to be supplemented by the following specific observations:

- The first of these stages would occur in detention, shortly before the subject's release. The administration of the substance would then constitute a treatment, designed to counteract new pathological sexual desires, that might arise right after release. This is why it is essential to reserve the products in question for inmates ending their sentence, save certain well monitored exceptional cases. This is simply an observation, and not an opinion. The National Consultative Ethics Committee is not competent to take a stand on the choice, the conditions and the value of a treatment. These are issues of deontology.

- The second stage would take the form of a trial, conducted under the conditions laid down by the law of December 20th 1988, and designed to gain knowledge of the substance's effects in the long term. In this respect, it should be noted that the trial, whatever the time at which it actually begins, should allow, on the one hand, for evaluation of the subject's chances of returning to some form of sexual normality, and on the other hand, for assessment of the product's potential for protecting society against the deviations in question. In fact, both the treated individual and potential victims threatened by his return to life outside prison are of interest for the research. In this sense, the trial is of direct social utility.

It must not be pretended that the administration of Androcur or Decapeptyl does not amount to control, and consequent adjustment of human behaviour. It would doubtless be excessive to speak of a "chemical strait jacket". Nevertheless, an individual put in these circumstances does find his behaviour transformed. To be sure, this occurs with his consent. But is he really in a position, at the time that he agrees, to assess all the consequences? In particular, does he fully understand that his sex life will not return to normal until after some tricky dose setting and manipulation, if then?

This is why one must insist on the need to obtain particularly well informed consent, and possibly even to envisage renewed consent. These observations are made solely with a view to concluding this answer with a counsel of particular prudence.

In summary, the circumstances in which administration of these substances can be considered are as follows:

1) Under no conditions should these substances be administered systematically during incarceration.

2) In the course of detention, these products are not to be prescribed in any guise other than treatment.

3) It is also and only as a form of treatment, that Androcur or Decapeptyl may be administered shortly before the subject's release.

4) After release, the products should not, as a general rule, be continued except within the framework of an experimental protocol.

The National Consultative Ethics Committee has pronounced itself in favour of this second approach.